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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,646	03/20/2002	Jan Van Der Greef	101137-31	6797
27387	7590	04/22/2004	EXAMINER	
BRUCE LONDA NORRIS, MCLAUGHLIN & MARCUS, P.A. 220 EAST 42ND STREET, 30TH FLOOR NEW YORK, NY 10017			DAVIS, DEBORAH A	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/980,646	<b>Applicant(s)</b> GREEF ET AL.	
	<b>Examiner</b> Deborah A Davis	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

1. Applicant's response to the office action mailed January 28, 2004 is acknowledged. Currently, claims 1-11 are pending and under consideration.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nedved et al (Characterization of Benzodiazepine "Combinatorial" Chemical Libraries by On-Line Immunoaffinity Extraction, Coupled Column HPLC-Ion Spray Mass Spectrometry – Tandem Mass Spectrometry, Analytical Chemistry, 1996, Vol. 68, pages 4228-4236).

Nedved et al anticipates the instant claims by teaching on-line detection methods comprising immunoaffinity extraction of analytes using reversed-phase HPLC columns coupled to a mass spectrometer (see abstract). Claim 1 is directed to adding a controlled amount of affinity molecule to an effluent followed by a separation step using a restricted-access support (see abstract). Nedved et al teaches antibodies to benzodiazepine were used to screen library components and were added to a Protein G column (effluent) wherein a pH change in the mobile phase eluted the benzodiazepine-antibody complexes on to a restricted access media column (support) thereby separating the selected benzodiazepine from the antibody (see abstract). The instant

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claim 1 also discloses a second step of separation whereby the analyte-affinity molecule complex is permeated flowed by a step to dissociate the analyte-affinity molecule complex followed by detection of the analyte using mass spectrometer. Nedved et al teaches a second step of backflushing the restricted access column (support) wherein the dissociated benzodiazepines analyte is eluted onto an analytical reversed phase column for separation and detection and characterization using mass spectrometry (see abstract and page 4229, column 2, paragraph 4). Claim 2 is directed to the use of a restricted access support in which the affinity molecule is retained followed by elution of the analyte to be detected by mass spectrometry. Nedved et al teaches a second separation step using restricted access column (support) wherein the antibody was retained after elution of the benzodiazepines analyte (page 4230, column 1 paragraph 1). Acetic acid was used to dissociate analytes with a pH of 7.4 as recited in claim 4 (page 4229, column 2, paragraphs 1-2 and page 4231 column 2, paragraph 1). The fractionation step used to separate the analytes were HPLC and other chemical combinatorial chemistry library systems as recited in claims 5 and 6 (see abstract and page 4229, column 1, paragraphs 1-2). Nedved et al discloses different instrumentation of mass spectrometer used in the detection of analytes such as MS/MS, tandem mass spectrometry and on line ion spray spectrometry as recited in claim 7 (page 4228, column 2, paragraph 2). The affinity proteins used were monoclonal and polyclonal antibodies to known benzodiazepine compositions as recited in claims 9 and 10. Known and unknown compounds such as pharamecueticals are detected by utilizing

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chemical libraries as taught by Nedved et al and as recited I claim 11 (page 4228, column 2, paragraph 1).

### ***Response to Arguments***

2. Applicant's arguments filed January 28, 2004 have been fully considered but they are not persuasive:

Applicant argues that the reference of Nedved et al does not anticipate the claimed invention because Applicant's on-line method is different from that of Nedved et al. Applicant further argues that all the steps in Nedved et al are not automated. This argument is not found persuasive because Applicant does not distinguish what steps are automated in his instant claims, therefore, the on-line method of Nedved et al meets this on-line requirement.

Applicant argues that the claimed method does not have all the steps the claimed method. Applicant argue that the claimed method form complexes between fractionated analyte effluent and putative receptors in solution and the resultant complexes are separated from the unbound analyte in a single step using a restricted-access medium. Applicant argue that, Nedved et al forms the benzodiazepine-IgG complexes as an insoluble immobile phase by first loading an analyte mixture onto a protein G agarose column that had already been saturated with anti-diazepine antibody. This argument is not found persuasive because Applicant is arguing limitations that are not found in the claims. The fact that the claimed method forms complexes between fractionated analyte effluent has not been distinguished in the claims. The claims does not

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distinguish whether the analyte was fractionated before the complex was formed or after. Nedved et al teaches that antibodies to benzodiazepine were added to an effluent and the complexes were eluted onto a restricted access media column, which meets the limitation of the instant claims (see page 4229, column 2, paragraph 4).

Applicant argues that after dissociating the putative receptor-analyte complexes, the claimed method employs one step to separate the putative affinity receptor from the dissociated analytes versus the method of Nedved et al that requires two separation steps. This argument is not found persuasive because the instant claims recite open language of "comprising" which does not exclude additional steps in a method.

Applicant argues that the reference of Nedved et al is not enabled for the instant claimed method because one of ordinary skill in the art could not reasonably combine the reference of Nedved et al and the description of the instant invention and be put in possession of the instant invention. This argument is not found persuasive because Applicant has presented no evidence or stated reasons why one of ordinary skill in the art would not be able to put the method of Nedved et al with the description of the instant invention to be put in possession of Applicant's invention - therefore, this argument is unfounded. For reasons stated above and of the previous Office Action, rejection of claims 1-11 are hereby maintained and made final.

### ***Conclusion***

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

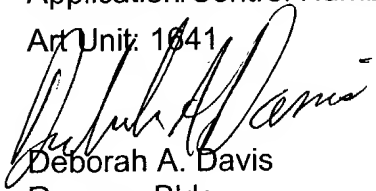
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

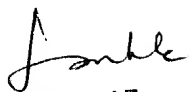
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